factor could be that three different assays with three different controls are involved.

Summary. We have shown that dimethyl succinate, dimethyl glutarate, and dimethyl adipate strongly attract the sawtoothed grain beetle in laboratory bioassays. However, these esters as isolated here from rolled oats are probably artifacts, whose formation was precipitated by the use of methanol in the isolation procedure.

Dimethyl glutarate enhances the attractancy of a wheat germ oil–oat oil–mineral oil mixture considerably when added to the mixture in 1.5–10.0 μL amounts. These chemically stable constituents may find applications as attractants, either alone or in conjunction with food-type stimuli now used with the Storgard cardboard monitoring trap.

ACKNOWLEDGMENT

The authors thank D. Weisleder for NMR spectra and R. E. England and R. D. Plattner for GC–MS determinations.

Registry No. Dimethyl glutarate, 1119-40-0; dimethyl succinate, 106-65-0; dimethyl adipate, 627-93-0.

LITERATURE CITED

Barak, A. V.; Burkholder, W. E. *Agric., Ecosyst. Environ.* **1985**, *12*, 207.

Dethier, V. G.; Brown, L. B.; Smith, C. N. *J. Econ. Entomol.* **1960**, *53*, 134.

Freedman, B.; Mikolajczak, K. L.; Smith, C. R., Jr.; Kwolek, W. F.; Burkholder, W. E. *J. Stored Prod. Res.* **1982**, *18*, 75.

Heydanek, M. G.; McGorrin, R. J. *J. Agric. Food Chem.* **1981a**, *29*, 950.

Heydanek, M. G.; McGorrin, R. J. *J. Agric. Food Chem.* **1981b**, *29*, 1093.

Likens, S. T.; Nickerson, G. B. *Proc. Am. Soc. Brew. Chem.* **1964**, 5–13.

Mikolajczak, K. L.; Freedman, B.; Zilkowski, B. W.; Smith, C. R., Jr.; Burkholder, W. E. *J. Agric. Food Chem.* **1983**, *31*, 30.

Mikolajczak, K. L.; Zilkowski, B. W.; Smith, C. R., Jr.; Burkholder, W. E. *J. Chem. Ecol.* **1984**, *10*, 301.

Nara, J. M.; Lindsay, R. C.; Burkholder, W. E. *J. Agric. Food Chem.* **1981**, *29*, 68.

Phillips, J. K.; Burkholder, W. E. *J. Econ. Entomol.* **1981**, *74*, 539.

Pierce, A. M.; Borden, J. H.; Oehlschlager, A. C. *Can. J. Zool.* **1981**, *59*, 1980.

Tamaki, Y.; Loschiavo, S. R.; McGinnis, A. J. *J. Agric. Food Chem.* **1971**, *19*, 285.

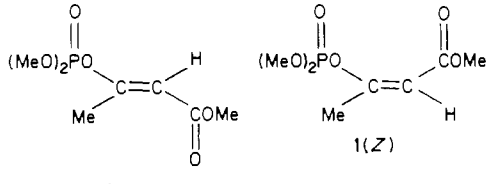
Received for review September 19, 1984. Revised manuscript received May 6, 1985. Accepted August 1, 1985. The mention of firm names or trade products does not imply that they are endorsed or recommended by the U.S. Department of Agriculture over other firms or similar products not mentioned.

β-Cyclodextrin Inclusion Complex of Mevinphos

Geoff Boocock and Patrick Camilleri*

Mevinphos [2-(methoxycarbonyl)-1-methylvinyl dimethyl phosphate] is a contact and systemic insecticide. The technical product contains at least 60% w/w and up to 20% w/w of the *E* and *Z* isomers, respectively. The *E* isomer is the more active ingredient. In this study, we report the selective inclusion of the *E* isomer in β-cyclodextrin to give a solid formulation that is insecticidally active and dissolves rapidly in water to give a clear solution.

Mevinphos was introduced by Shell Development Co. in 1953 under the trade name Phosdrin and is now a well established organophosphorus insecticide with a wide range of activity. It is fast acting and highly effective at low dosage rates (Shell International Chemical Co., 1976). Phosdrin is water miscible and systemic in plants and also has fumigant, acaricidal, and ovicidal properties. The active component in Phosdrin is 2-(methoxycarbonyl)-1-methylvinyl dimethyl phosphate (1) which can exist as the *E* isomer, mp 21 °C, or as the *Z* isomer, mp 7 °C. Phosdrin contains at least 60% w/w and up to 20% w/w of the *E* and *Z* isomers, respectively.



Phosdrin has a high mammalian toxicity both orally (rat LD_{50} = 2.9–12 mg/kg) and percutaneously (rat LD_{50} = 1.9 mg/kg) (Shell International Chemical Co., 1976). The percutaneous toxicity is also high when the toxicant is formulated as an emulsifiable concentrate. Transformation of liquid Phosdrin into a solid form that could be formulated as pellets or granules should make it much safer to handle during the preparation of the spray liquid. During our search for such a formulation we discovered that treatment of Phosdrin with a solution of β-cyclodextrin in water gave rise to an inclusion complex that contained exclusively the *E* isomer. This form of encapsulated 1 showed excellent insecticidal activity. In this text we shall refer to the encapsulated form of Phosdrin in β-cyclodextrin by the abbreviation PCDC (Phosdrin cyclodextrin cryptate).

Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, U.K.

EXPERIMENTAL SECTION

Synthesis of Phosdrin β-Cyclodextrin Cryptate. β-Cyclodextrin (8.2 g) was dissolved in distilled water (100 mL) at 59 °C. The warm solution was slowly treated dropwise with stirring with technical Phosdrin (17.2 g). The mixture was cooled in an ice bath with continued stirring for 3 h. The white precipitate formed was filtered off, washed with ice water (3 × 7 mL), and dried in a desiccator to give a yield of 9.1 g of PCDC.

Analyses. *Chromatography.* Phosdrin was analyzed by gas–liquid chromatography with a flame ionization detector. The separation of the *E* and *Z* isomers was

0021-8561/85/1433-1032$01.50/0

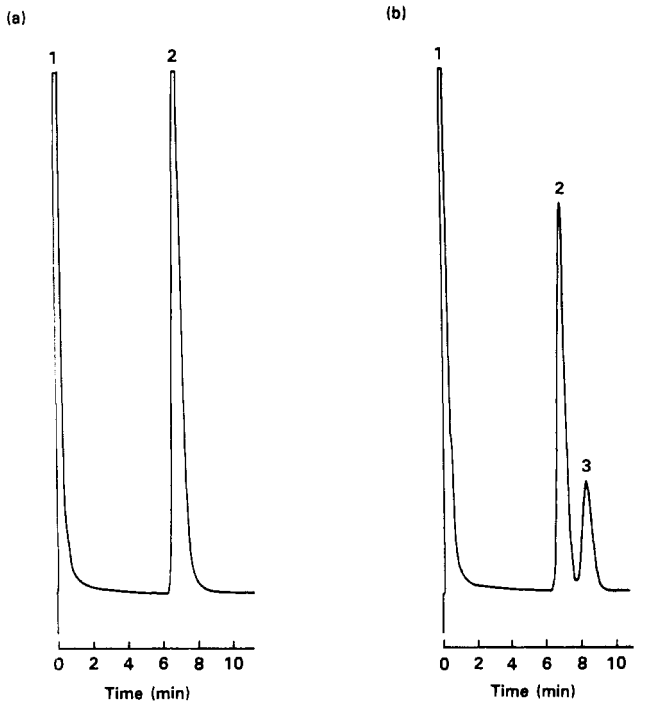


Figure 1. GC analysis of 1. Chromatogram a: PCDC in acetone. Chromatogram b: technical Phosdrin in acetone. Identification: 1, acetone; 2, *E* isomer; 3, *Z* isomer.

carried out on a glass column (1.0 m × 3 mm i.d.) packed with Reoplex 400 stationary phase using nitrogen (0.09 L/min) as carrier gas. The column temperature was kept at 145 °C. Under these conditions isomers *E* and *Z* had retention times of 7.0 and 8.4 min, respectively (Figure 1). For the analysis of the Phosdrin content in PCDC about 0.1 g was shaken with Analar acetone (5 mL). This treatment released the Phosdrin quantitatively from the cyclodextrin complex into the acetone, which was then analyzed as above. β-Cyclodextrin itself is essentially insoluble in acetone.

Spectroscopy. Nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a 360-MHz Fourier transform instrument; samples were dissolved in Me_5SO-d_6, and tetramethylsilane was used as the internal standard.

Biological Activity. The activity of PCDC against the black bean aphid *Aphis fabae* was investigated under laboratory conditions relative to that of a standard Phosdrin 240 g/L, water-soluble concentrate (WSC). Pairs of excised broad bean leaves were sprayed by an Oxford precision sprayer at a volume rate equivalent to 340 L/ha, with a suitable series of dilutions. Leaf tissue was infested with aphids at intervals of 1, 2, and 5 h after spraying. Mortality was assessed after 24 h.

RESULTS AND DISCUSSION

Both chromatographic (Figure 1) and spectral (Figure 2) analyses of PCDC indicated that the β-cyclodextrin cavity could only accommodate the *E* isomer of 1. The composition of this complex was found to be about 14% *E* isomer, 16% water, and 70% β-cyclodextrin.

β-Cyclodextrin has been used previously for the separation of positional isomers (Kazutoshi, 1977) and for the resolution of chiral compounds (Mikolajczyk and Drabowicz, 1978). As 1 is a relatively polar molecule, separation of the *E* and *Z* isomers (via the preferential formation of an inclusion complex by the former isomer) is most probably due to factors such as hydrogen-bond formation and dipole–dipole interactions (Saenger, 1976).

PCDC showed good storage stability. After 2 weeks at 35 and 45 °C, the content of 1 in the β-cyclodextrin decreased by 4 and 10%, respectively. It also had excellent water solubility and dissolved rapidly in water to give a clear solution.

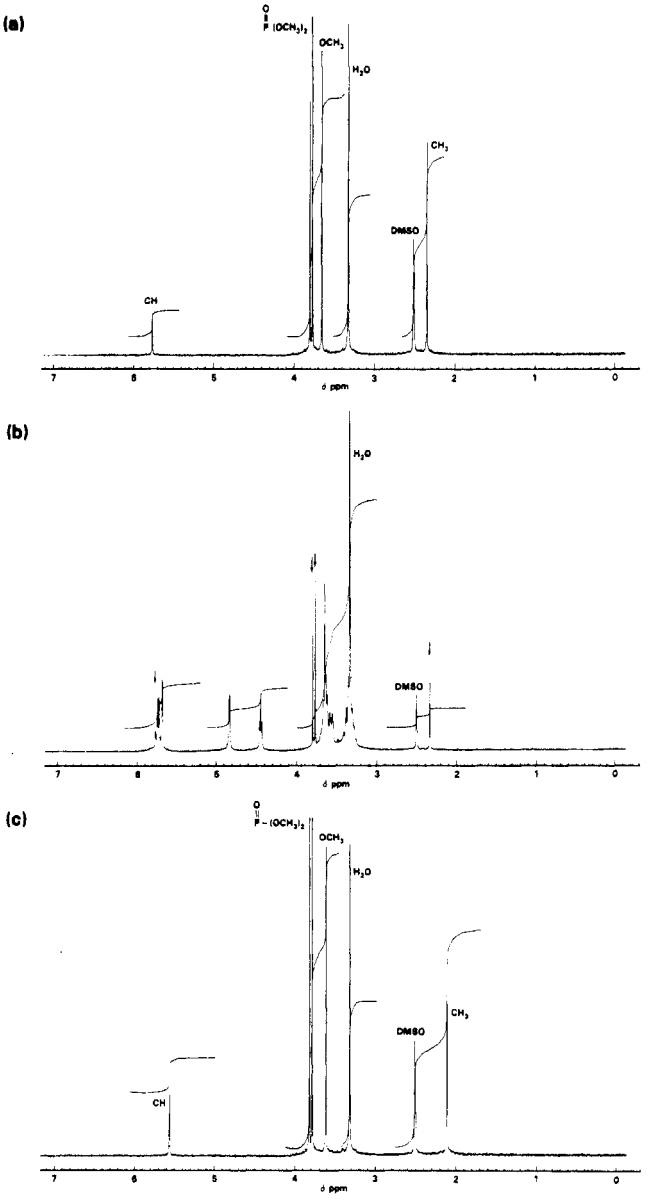


Figure 2. NMR spectra in Me_2SO-d_6: (a) *E* isomer of 1; (b) PCDC; (c) *Z* isomer of 1. The arrowed (↓) peaks in spectrum (b) demonstrate the presence of isomer *E* only; the other peaks result from the protons in β-cyclodextrin.

Table I. Activity of Mevinphos Formulations against *Aphis fabae*

treatment	hours after spraying	24-h LC_{50} (% act. matl)
PCDC (14% *E* isomer)	1	0.00066
	2	0.00045
	5	0.00090
phosdrin (240 g/L WSC; equivalent to 14.4% *E* isomer)	1	0.0011
	2	0.00044
	5	0.0012

Data comparing the insecticidal efficacy of PCDC with that of a 240 g/L standard formulation of Phosdrin (WSC) are presented in Table I. The 240 g/L WSC contained a minimum of 144 g/L of the *E* isomer, i.e. approximately 14.4 g/100 g of formulation. The insecticidal activity of this isomer is about 100 times greater on molar basis (Casida et al., 1956) than that of the *Z* isomer, which, of course, is also present in the formulation. Table I therefore

shows that the insecticidal effectiveness of the cyclodextrin formulation is at least equal to that of the standard WSC formulation. However, the formulation of Phosdrin as the β-cyclodextrin cryptate would only be attractive economically if the cost of β-cyclodextrin decreased appreciably.

ACKNOWLEDGMENT

The authors thank M. Pinnegar for his interest in this work, Dr. C. Bimson for the analytical measurements, and J. S. Badmin for the evaluation of biological activity.

Registry No. Mevinphos, 7786-34-7; β-cyclodextrin, 7585-39-9; PCDC, 98838-08-5.

LITERATURE CITED

Casida, J. E.; Gotterdam, P. E.; Getzin, L. W., Jr.; Chapman, R. K. *J. Agric. Food Chem.* **1956**, *4*, 236.
Kazutoshi, Y. Jpn. Kokai 77 42825; *Chem. Abstr.* **1977**, *87*, 134490*q*.
Mikolajczyk, M.; Drabowicz, J. *J. Am. Chem. Soc.* **1978**, *100*, 2510.
Saenger, W. In "Environmental Effects of Molecular Structure and Properties"; Pullman, B., Eds.; D. Reidel Publishing Co.: Dordrecht, Holland, 1976; pp 265–305.
Shell International Chemical Co. "Chemicals for Plant Protection, Veterinary Uses and Public Health"; Butler and Tanner Ltd.: London, 1976; p 49.

Received for review February 5, 1985. Accepted July 2, 1985.

Development of Insect Juvenile Hormone Active Oxime *O*-Ethers and Carbamates

Akira Nakayama, Hajime Iwamura,* Atsushi Niwa, Yoshiaki Nakagawa, and Toshio Fujita

Results of previous quantitative structure–activity relation analyses of insect juvenile hormone active compounds prompted us to design undecen-2-one oxime *O*-ethers and undecen-2-yl carbamates. Their activities against *Culex pipiens* (common mosquito), *Chilo suppressalis* (rice stem borer), and *Musca domestica* (housefly) were comparable to that of naturally occurring JH I. To produce higher activities, we hybridized the structures of the oxime *O*-ethers and the reportedly highly active 2-(4-phenoxyphenoxy)ethyl carbamates and obtained compounds whose activities against *C. pipiens* were comparable to the 90–100% inhibition of metamorphosis by methoprene, the most highly active of the JH mimetic compounds.

The juvenile hormones (JH) have long been considered as a rational source for the design of a new regulator of insect growth. With the aim of less costly synthesis and more field stability than is possible with natural juvenile hormones, we prepared and tested a number of analogous compounds for their activities against various insect species, on the assumption that structural mimicry also mimics activity. Knowledge of what structural essentials confer the activity of an already known series of compounds should be very useful for this purpose. Quantitative structure–activity relation (QSAR) analysis also should be an efficient research tool. In recent analyses of JH activity against two insect species, *Aedes aegypti* (yellow fever mosquito) and *Tenebrio molitor* (yellow mealworm), by natural JHs and a related 2,4-dodecadienone series of compounds (Nakayama et al., 1984), we found that the steric dimensions and hydrophobicity of the molecule are important factors in the governing of JH activity.

From these results and the assumption that information on the structure vs. activity relation of one class of compounds is applicable to other types of compounds, we designed undecen-2-one oxime *O*-ether and undecen-2-yl carbamate structures. These compounds have been proved as active as JH I against *Culex pipiens* (common mosquito) and *Chilo suppressalis* (rice stem borer) and to be much more active than JH I against *Musca domestica* (housefly). Their structure–activity profiles were collated with previous QSAR results, providing further evidence of common structural features that confer JH activity throughout insect species. To obtain higher activity, we hybridized the structures of the oxime *O*-ethers and the reportedly highly active 2-(4-phenoxyphenoxy)ethyl carbamates (Karrer and Farooq, 1981) to produce (4-phenoxyphenoxy)- and (4-benzylphenoxy)acetaldehyde oxime *O*-ethers and related compounds. The activity of some of these substances on *C. pipiens*, in terms of 90–100% inhibition of metamorphosis, was as potent as, or slightly less potent than, methoprene, the most active of the JH mimetic compounds known so far.

Department of Agricultural Chemistry, Faculty of Agriculture, Kyoto University, Kyoto 606, Japan.

EXPERIMENTAL SECTION

^{1}H NMR spectra were obtained in CCl_4 or $CDCl_3$ with tetramethylsilane as the internal reference in a JOEL PMX-60 spectrometer. IR spectra were recorded on a Shimadzu IR-27G spectrometer.

(3*E*)-6,10-Dimethyl-3,9-undecadien-2-ol (3a). (3*E*)-6,10-Dimethyl-3,9-undecadien-2-one (**2a**; 19.4 g, 0.1 mol) was added in drops to a suspension of $LiAlH_4$ (1.9 g, 0.05 mol) in dry ether (140 mL) at −7 °C over a period of 0.5 h. After this combination was stirred for 10 min at the same temperature, ether saturated with water was added to the reaction mixture which was kept below −5 °C. The white precipitate was removed by filtration through Celite. The filtrate was washed with water, dried over $MgSO_4$, and concentrated in vacuo, giving a colorless oil. This oil was applied to a silica gel column that then was treated with 20% ethyl acetate in *n*-hexane, giving 15.0 g (77%) of **3a**: ^{1}H NMR ($CDCl_3$) δ 4.18 (m, 1, CHOH), 5.00 (br t, 1, J = 7 Hz, CH=C(CH_3)$_2$), 5.35 (m, 2, CH=CH); IR (film) 3350 (OH) cm^{-1}.

(3*E*)-6,10-Dimethyl-3-undecen-2-ol (3b). (3*E*)-6,10-Dimethyl-3-undecen-2-one (**2b**; 8.7 g, 0.044 mol) was reduced by the same procedure essentially as that described

0021-8561/85/1433-1034$01.50/0